September 9, 1998

This document was submitted to EPA by a registrant in connection with EPA's evaluation of this chemical and it is presented here exactly as submitted.

Bayer

August 20, 1998

Agriculture Division

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DEF Chemical Review Manager
Accelerated Reregistration Branch
Special Review and Reregistration Division (H7508W)-
Office of Pesticide Programs
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401 M St., S.W.
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Attention: Mr. Tom Luminello, DEF Chemical Review Manager, Accelerated Reregistration Branch

Subject: Comments on Draft Chapters of the Tribufos Reregistration Eligibility Decision. List B, Case 2145

Dear Mr. Luminello:

On July 20, 1998 Bayer Corporation received copies of draft chapters of the Health Effects Division and Ecological Effects and Environmental Fate Division chapters of the tribufos Reregistration Eligibility Decision (RED). As mentioned in the letters dated July 20, 1998 and August 13, 1998 from Jack E. Housenger of EPA to Brian Dehart of Bayer Corporation, we are providing comments on errors and other issues noted in the RED.

It is important for the Agency and any reader of this document to know that although DEF (tribufos) is classified as an organophosphate it is not an insecticide. Its only registered use is on cotton as a defoliant. Defoliation facilitates cotton harvest by removing the leaves. DEF provides the cotton grower a cheap and effective means of defoliation.

The comments listed below address three sections of the Health Effects Divisions chapter: Dietary Risk Assessment, Occupational Exposure Assessment, and Toxicological Endpoints. Last, the Environmental Fate and Ecological Effects chapter is discussed.

Dietary Risk Assessment

The EPA's Health Effects Division chapter of the RED for tribufos (DEF) included a dietary exposure risk assessment. This assessment was based on data generated in a cotton metabolism study (MRID 42350009) performed in a greenhouse at an application rate three times higher than permitted by the DEF label. The purpose of the high application rate in the cotton

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metabolism study was to facilitate identification of residues, not to quantitate residues. No correction was performed in the Agency's calculations to account for the exaggerated application rate at which this study was performed. Consequently, the residue levels from this study which were used in the Agency's dietary risk assessment were much to high. However, EPA has in its files actual cotton magnitude of the residue data (MRID 44439201 submitted on December 2, 1997) from field trials performed at maximum application rates as permitted by the DEF label. The Agency should use this data in acute and chronic dietary risk assessments. The results of the Agency's dietary risk assessment are unrealistic and indicate a much greater risk than when the cotton magnitude of residue data are used. The Agency's calculations, which are based on studies not intended to be used in a dietary risk assessment, greatly overestimate the percent of the reference dose (% RfD) consumed by various populations. The values EPA calculated were: U.S. Population, 254%; Hispanics, 305%; Children (1-6 years), 585%; Children (7-12 years) 401%; and Non-nursing Infants (<1 year), 749%.

Refined Tier III calculations performed by Bayer Corporation scientists, based on the cotton magnitude of the residue data (MRID 44439201) in the Agency's files indicates that the % RfD actually consumed for various populations is: U.S. Population, 5%; Hispanics, 5%; Children (1-6 years), 16%; Children (7-12 years) 9%; and Non-nursing Infants (<1 year), 10%. The Agency has no concern for exposures less than 100% of the RfD.

Similarly, the Agency's calculation of the margins of exposure (MOEs) for acute exposure based on this same cotton metabolism data were: U.S. Population, 625; Infants (<1 year), 333; Children (1-6 years), 333; Females (13+ years), 1250; and Males (13+ years), 1000.

Refined probabilistic (Monte Carlo) Tier III calculations performed by scientists at Bayer Corporation, based on the actual magnitude of the residue data (MRID 44439201) already submitted to the Agency show the correct MOEs to be: U.S. Population, 9217; Infants (<1 year), 4139; Children (1-6 years), 6487; Females (13-50 years), 22378; and Males (13-19 years), 17832. The Agency has no concern for MOEs greater than 1000. Clearly, use of the appropriate data and refined risk assessment calculations demonstrate that tribufos poses no acute or chronic dietary risk to humans from exposure at anticipated residue levels.

Two mathematical errors were found in the Agency's calculations:

1) The calculated anticipated residues in cotton Raw Agricultural Commodities were based on a cotton metabolism study application rate which is three times higher than the rate permitted on the DEF label. If these values are to be used to calculate dietary exposure (Bayer Corporation opposes this) then they should have been corrected for this dose exaggeration. Rather than using a residue value of 200 ppm for cotton gin byproducts, the Agency should have divided the measured residue of 175 ppm by three (175/3 = 58

ppm) or at least have indicated that the residue levels and resulting dietary exposure are too large by some but unknown amount.

2) The dose exaggeration used in the cotton metabolism study (3X) should have been reflected in the calculation of the 1X dietary burden for the cattle feeding study (MRID 43821601). Based on metabolism data, the 1X cattle dietary burden would be 15 ppm. The cattle feeding study was conducted at feed residue levels of 9 ppm, 33 ppm, and 120 ppm, corresponding to 0.6X, 2.2X, and 8X, respectively, which were appropriate feeding levels.

Occupational Exposure Assessment

Regarding the evaluation of occupational exposures to tribufos, Bayer submitted the reports of 2 studies to EPA in 1993, a mixer/loader/applicator exposure study (MRID 42685901) and a harvester exposure study (MRID 42701601). Both studies were conducted in response to an EPA Data Call-In and the data from these studies provide the primary basis for EPA's evaluation. However, the EPA's evaluation contains a number of errors in the transcription and/or use of the data, including the calculation of exposures on a µg/lb AI basis, the calculation of transfer coefficients on a 50 gm/hr basis, and the best fit dislodgeable residue values on a µg/50 gm basis. In addition, the evaluation incorrectly assumes that the exposure data are normally distributed and uses the arithmetic mean as a measure of central tendency rather than the geometric mean which provides a more representative measure of central tendency for log-normally distributed data. The evaluation also incorrectly states that the reason the blood cholinesterase activity of mixer/loader/applicators and harvesters was evaluated in the Bayer studies was that it is required by CDPR. In fact the plasma and erythrocyte cholinesterase activity of all workers in these studies was measured during the entire tribufos use season as an inherent part of Bayer's overall evaluation strategy. Bayer discussed in detail the purpose and value of the cholinesterase monitoring strategy with EPA and CDPR prior to the conduct of the study. The results clearly indicate there were no exposure-related effects associated with tribufos under actual use conditions. As such, Bayer believes that tribufos has been and can continue to be used safely.

Toxicological Endpoints

Bayer concurs with EPA's assessment that tribufos is not a developmental or a reproductive toxicant. The developmental toxicity studies and the two-generation reproduction study revealed no evidence of increased sensitivity of developing fetuses or pups. Thus, the 10-fold FQPA uncertainty factor for enhanced sensitivity of infants and children should not be retained. Bayer also concurs with the EPA's assessment that tribufos is not a mutagenic toxicant. A complete battery of *in vitro* and *in vivo* mutagenicity studies have been performed on tribufos

and all studies were unequivocally negative, demonstrating that tribufos is not mutagenic.

Bayer respectfully disagrees with the EPA's determination that the cholinesterase LOEL from a 21-day dermal toxicity study is the toxicological endpoint which should be used in risk assessments for short-term and intermediate-term dermal exposures to tribufos. Although this is an important study to consider, there are other studies, including a dermal absorption study using the formulated product, which should be used in risk assessments for dermal exposures to tribufos. The study EPA selected as providing the relevant toxicological endpoint was performed with technical grade tribufos, which is a manufacturing-use product. Workers mixing, loading or applying tribufos use the end-use product, DEF 6. Thus, the dermal absorption study on DEF 6 is a critical study which should be used with NOELs from repeated-dose toxicity studies to evaluate the hazard from short and intermediate-term exposures to tribufos (DEF 6).

Ecological Effects and Environmental Fate

The EFED RED Chapter for Tribufos erroneously identified a risk of chronic and reproductive effects to birds. It is the position of Bayer Corp. that avian species are not exposed to significant tribufos residues on a chronic basis. The nature of the product, DEF, is to desiccate and defoliate cotton plant leaves within 14 days of application. Prior to cotton harvest, the cotton leaves die, dry up, fall to the ground and decay very rapidly. It is therefore very unlikely that treated vegetation would be used as an avian food item in the fall after cotton harvest, and it is impossible for this to occur during the following spring when avian breeding recurs. Any food items obtained the following spring from fields treated with tribufos the previous year, would have trace concentrations of tribufos and would not pose a chronic or reproductive risk to birds.

Typical agricultural practices used for cotton are important considerations when assessing avian chronic risk. DEF applications are made at the end of the cotton growing season which would be in August through November across the United States. Harvest occurs 14 days after the DEF application; from early August to early December. Once harvest is complete, typical agricultural practice is to shred and destroy the remaining cotton plant branches and root structure as soon as possible.

This cotton field transition, from DEF application, to harvest, to a fallow field and finally to another crop is driven by pest management, economic and weather factors. In most areas of the country the cotton farmers immediately disk in the remaining cotton branches, dead leaves, and root structure to a depth of at least 6 inches. This process ensures that boll worms do not over winter in the cotton fields. In most regions of the country this pest management practice is mandated by law to prevent boll worm infestations. This cotton field transition also allows the

farmer to efficiently and effectively prepare the soil for over wintering or for the next crop. The destruction of the plant and preparation of the field is completed before the winter rainy season. Since the cotton plant is hardy and it's branches and root structure are left in the field after harvest, it is to the farmer's advantage to speed up the degradation of the shredded plant material by exposing it to the soil, winter rains, and natural weathering.

Typically, the field transition is completed and a new crop is planted in December through March. The next crop planted may be cotton, corn, fall vegetables, soybeans or peanuts, depending upon the region of the country. This replanting further decreases the likelihood of contaminated, avian food items being available in the Spring.

For the reasons stated above, any cotton plant debris that may remain, typically a few bits of decaying branches, would have been disced into the soil at a depth of 6 inches or greater long before the Spring. These physical and mechanical farm activities such as leaf desiccation, plant shredding and destruction, and soil discing, would redistribute tribufos residues into the soil. Even in the absence of any chemical degradation, the concentration in the soil would be low and not present a hazard to breeding birds. For example, if the maximum application rate was applied (1.875 lb a.i./acre), the application efficiency was 100% (all of it was deposited on the target field), all of this pesticide mass was mechanically mixed into the top 6-inches of soil, and no chemical degradation were to occur, the estimated tribufos concentration in the soil would be about 1 ppm (calculation assumes a soil bulk density of 1.2 g/cm3). This is also a conservative estimate of the maximum concentration in avian food items found in or on this soil (e.g., weed seeds, earthworms, etc.). Since this concentration is more than 100 times less than the chronic/reproductive no effect level (148 ppm), these residues clearly pose a negligible risk to birds.

Yours very truly,

BAYER CORPORATION
AGRICULTURE DIVISION

John S. Thornton
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and Regulatory Affairs
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